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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,884	02/19/2004	Randy Scott	GHI-0007.US (GHDX-007)	2652
80811 7590 09/29/2009 Genomic Health, Inc. c/o Kathleen Determann 301 Penobscot Road Redwood City, CA 94063				
EXAMINER WOOLWINE, SAMUEL C				
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1637				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/783,884

Applicant(s)

SCOTT ET AL.

Examiner

SAMUEL WOOLWINE

Art Unit

1637

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 104, 106-108 and 110-113 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 104, 106-108 and 110-113 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/888)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status

Applicant's reply filed 05/26/2009 has been considered. Claims 104, 106-108 and 110-113 are pending and under consideration.

Regarding the objections/rejections made in the Office action mailed 02/26/2009, the objection to claim 104 is withdrawn in view of amendment.

The rejection of claims 104, 110, 112 and 113 under 35 USC 102(b) over Lipson et al is withdrawn in view of Applicant's amendment to claims 104 (from which claims 112 and 113 depend) and 110 to require step (d), which is not taught by Lipson.

The rejection of claims 104, 106-108 and 111-113 under 35 USC 103(a) over Danenberg et al (US 2002/0009795) in view of Duvick (US 7.026,123), Clement et al (Journal of Biological Chemistry, 276(20)16919-30 (2001)), Lipson et al (PNAS 86:9774-7 (1989)), Chang et al (Journal of Neuroscience Methods 94:177-85 (2000)) and Matsubara et al (Endocrinology 138(11):5075-8 (1997)) is withdrawn in view of Applicant's amendment. Danenberg did not expressly teach step (d) (comparing the expression of the target gene to data based on patients of "known clinical outcome").

New rejections are set forth below necessitated by the amendment to claims 104 and 110.

To the extent Applicant's arguments apply to the new rejections, the arguments will be addressed following the rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 104, 106, 108 and 110-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dai et al (US 2003/0224374, prior art of record) in view of Duvick (US 7,026,123, prior art of record), Clement et al (Journal of Biological Chemistry, 276(20):16919-30 (2001), cited on the IDS of 05/20/2005), Lipson et al (PNAS 86:9774-7 (1989), prior art of record), Chang et al (Journal of Neuroscience Methods 94:177-85 (2000), prior art of record) and Matsubara et al (Endocrinology 138(11):5075-8 (1997), prior art of record).

With regard to claims 104 and 110, Dai taught *hybridizing a polynucleotide complementary to an RNA sequence of a target gene to RNA from a tissue sample that*

has been obtained from a human subject with cancer, or a nucleic acid produced therefrom, to form a complex...

Figure 2 and paragraph [0027] for example, where Dai taught hybridizing nucleic acid produced from RNA from tumor tissue samples to microarrays and measuring mRNA transcript abundance. See also paragraph [0093] where Dai taught that the sample could be taken from an individual afflicted with breast cancer, and that the individual could be a human. Dai also taught at paragraph [0093] that the mRNA or nucleic acids derived therefrom could be labeled and hybridized to an array. With regard to claim 110, the probes on a microarray are "immobilized on a solid support".

quantitating the complex to determine the expression level of the target gene...

Paragraph [0027]: "measuring differential changes in mRNA transcript abundance". Paragraph [0188]: "Fluorescence intensities on scanned images were quantified, normalized and corrected."

normalizing the expression level of the target gene relative to the expression level of one or more reference genes in the tissue sample to determine a normalized expression level of the target gene...

Paragraphs [0119]-[0120] (emphasis provided):

[0119] In using the markers disclosed herein, and, indeed, using any sets of markers to differentiate an individual having one phenotype from another individual having a second phenotype, one can compare the absolute expression of each of the markers in a sample to a control; for example, the control can be the average level of expression of each of the markers, respectively, in a pool of individuals. To increase the sensitivity of the comparison, however, the expression level values are preferably transformed in a number of ways.

[0120] For example, the expression level of each of the markers can be normalized by the average expression level of all markers the expression level of which is determined, or by the average expression level of a set of control genes. Thus, in one embodiment, the markers are represented by probes on a microarray, and the expression level of each

of the markers is normalized by the mean or median expression level across all of the genes represented on the microarray, including any non-marker genes. In a specific embodiment, the normalization is carried out by dividing the median or mean level of expression of all of the genes on the microarray. In another embodiment, the expression levels of the markers is normalized by the mean or median level of expression of a set of control markers. In a specific embodiment, the control markers comprise a set of housekeeping genes. In another specific embodiment, the normalization is accomplished by dividing by the median or mean expression level of the control genes.

comparing the normalized expression level of said target gene to data based on normalized expression of the target gene in cancer tissue samples obtained from patients of known clinical outcome...

Paragraph [0114] (emphasis provided):

[0114] The present invention provides sets of markers useful for distinguishing samples from those patients with a good prognosis from samples from patients with a poor prognosis. Thus, the invention further provides a method for using these markers to determine whether an individual afflicted with breast cancer will have a good or poor clinical prognosis. In one embodiment, the invention provides for method of determining whether an individual afflicted with breast cancer will likely experience a relapse within five years of initial diagnosis (i.e., whether an individual has a poor prognosis) comprising (1) comparing the level of expression of the markers listed in Table 5 in a sample taken from the individual to the level of the same markers in a standard or control, where the standard or control levels represent those found in an individual with a poor prognosis; and (2) determining whether the level of the marker-related polynucleotides in the sample from the individual is significantly different than that of the control, wherein if no substantial difference is found, the patient has a poor prognosis, and if a substantial difference is found, the patient has a good prognosis. Persons of skill in the art will readily see that the markers associated with good prognosis can also be used as controls. In a more specific embodiment, both controls are run. In case the pool is not pure 'good prognosis' or 'poor prognosis', a set of experiments of individuals with known outcome should be hybridized against the pool to define the expression templates for the good prognosis and poor prognosis group. Each individual with unknown outcome is hybridized against the same pool and the resulting expression profile is compared to the templates to predict its outcome.

determining cancer prognosis or prediction for the human subject based on results obtained from step (d) [the comparing step]...

Paragraph [0114] (see above).

With regard to claims 106 and 108, Dai taught (paragraph [0093]) that the sample could be from an individual with breast cancer and could be a tumor biopsy.

With regard to claim 112, since Dai derived the set of markers from human genes (paragraph [0060]: "Each markers correspond to a gene in the human genome..."), and taught assessing the expression of these markers in humans (paragraph [0093] for example), one of skill in the art would clearly have recognized the method applied to "human genes".

With regard to claim 113, Dai taught (paragraph [0133]): "In a specific embodiment, the invention provides for oligonucleotide or cDNA arrays comprising probes hybridizable to the genes corresponding to each of the marker sets...". See also paragraph [0144] where Dai taught making probes for microarrays.

With regard to claims 104 and 110, Dai did not teach targeting *intronic* sequences; i.e. Dai did not teach that the probes of the microarray were designed to hybridize to *intronic RNA* or nucleic acids produced therefrom.

With regard to claim 111, Dai did not teach quantitative PCR using a primer complementary to an intronic RNA sequence.

With regard to claims 104 and 110, Duvick taught methods for examining the effects of transforming clones of nucleic acid sequences into host cells, where each clone comprised a candidate sequence and a "U-tag", a short, random nucleotide sequence (see column 5, lines 17-28). Duvick taught that the U-tag may "be designed into an intron sequence that occurs anywhere within a transcript" (column 5, lines 59-60). Duvick stated (column 5, line 65, citing Clement): "In this design, the spliced-out intron RNA would be detected at a level proportional to the transcription rate. Recent data from mammalian cells indicates that intron RNAs, after splicing, persist in the cell

with reasonable half-lives, contrary to what was previously thought." The point is, Duvick suggested that introns could be detected, and that the level of the detected intron correlated with transcription rate (i.e. expression).

With regard to claims 104 and 110, Clement stated:

"A widely held belief is that spliced introns accumulate at low levels because they are rapidly degraded (within seconds) at their site of origin in the nucleus (14, 22). However, there is little direct evidence to support this view. The only mammalian intron whose fate and stability have been examined in detail is the IVS_{ICB1} intron from a mouse T-cell receptor (TCR)¹- β gene. This intron is easily detectable by the relatively insensitive Northern blot procedure, despite being generated from only a modestly transcribed gene (23)." (1st full paragraph, page 16920)

"Because the Pem gene is not cell type-specific and its introns appear to be typical, we hypothesized that Pem would be a good candidate to provide information on the metabolism of mammalian introns in general." (2nd full paragraph, page 16920)

"Our analysis of the three introns in the Pem coding region revealed that they had a range of half-lives that were even longer than that of the only other previously analyzed vertebrate intron, IVS_{ICB1}." (3rd full paragraph, page 16920)

Thus Clement taught that introns from the Pem gene, which appear to be typical introns, are more stable (longer half-lives) than the IVS_{ICB1} intron, which was detectable by the "relatively insensitive Northern blot procedure".

With regard to claims 104 and 110, Lipson taught detecting levels of TK (human thymidine kinase) expression by subjecting total RNA to RT-PCR and detecting the resulting product on a Southern blot. Lipson used an intron-specific probe. See entire article, especially figures 1 and 2.

With regard to claims 104 and 110, Matsubara taught quantitative analysis of GH (growth hormone, rat) pre-mRNA expression using an intron-specific competitive PCR method (see page 5076, figure 1 and column 1). With regard to claim 111, Matsubara taught quantitative PCR using a primer complementary to intronic RNA (page 5076, column 1, first paragraph).

Chang taught a method of analyzing tyrosine hydroxylase (rat) transcription using an intron-specific probe by RNase protection (see section 2.2, page 178) and in situ hybridization (see section 2.4, page 180). Chang cited other studies that have successfully used intron-specific in situ hybridization to detect rat vasopressin/neurophysin I, corticotrophin releasing hormone, neurotensin, and gonadotropin releasing hormone (see second paragraph, section 4, page 184). Chang noted (last paragraph, page 184, citations omitted, emphasis provided):

Based on the present results, together with previous work on the expression of neuropeptide genes, we conclude that estimates of transcription rates for the TH gene based on relative levels of intron 2 sequences are well founded. The logical extension and underlying rationale of the present study is the application of intron-specific in situ hybridization analysis for studies on TH gene expression within neural tissues where nuclear run-on assays or RNase protection are not possible because of reasons of sensitivity or that the preservation of anatomical information is important.

It would have been *prima facie* obvious to one of ordinary skill in the art to modify the method suggested by Dai by measuring expression based on the detection of intron sequences as suggested by Duvick. In fact the disclosures of Lipson, Matsubara and Chang all used intron-specific primers or probes to quantify gene expression. The disclosures of Clement, Lipson, Matsubara and Chang provided a reasonable expectation of success in quantitatively detecting intron sequences as a measure of gene expression. Based on the disclosures of Clement, Lipson, Matubara and Chang, one of skill in the art would have had a reasonable expectation of success in detecting intron sequence, a reasonable expectation of success that the levels of detected intron sequence would be proportional to the transcription rate, which is a measure of gene expression, and a reasonable expectation of success in quantitatively detecting the sequences given the quantitative densitometry taught by Lipson and the quantitative

PCR taught by Masubara. Furthermore, one would have had a reason to use intron sequences because based on the disclosures of the cited references, intron sequences would have been clearly obvious alternatives to exon sequences in measuring gene expression.

It would also have been obvious to use intron-specific primers to perform quantitative PCR to assess the level of gene expression as taught by Matsubara, since Dai taught that "[t]he expression levels of the marker genes in a sample may be determined by any means known in the art" (paragraph [0127]). One of skill in the art would have appreciated that Matsubara's method of competitive PCR using intron-specific primers was merely another means known in the art to quantify the level of a particular RNA in a sample.

Claim 107 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dai et al (US 2003/0224374) in view of Duvick (US 7,026,123, prior art of record), Clement et al (Journal of Biological Chemistry, 276(20)16919-30 (2001), cited on the IDS of 05/20/2005), Lipson et al (PNAS 86:9774-7 (1989), prior art of record), Chang et al (Journal of Neuroscience Methods 94:177-85 (2000), prior art of record) and Matsubara et al (Endocrinology 138(11):5075-8 (1997), prior art of record) as applied to claims 104, 106, 108 and 110-113 above, and further in view of Danenberg (US 2002/0009795, prior art of record).

The teachings of Dai, Duvick, Clement, Lipson, Chang and Matsubara have been discussed. These references did not teach or suggest a FFPE sample as recited in claim 107.

Danenberg taught (paragraph [0009]): "Until now, quantitative tissue gene expression studies including those of TS expression have been limited to reverse transcriptase polymerase chain reaction (RT-PCR) amplification of RNA from frozen tissue. However, most pathological samples are not prepared as frozen tissues, but are routinely formalin-fixed and paraffin-embedded (FFPE) to allow for histological analysis and for archival storage...Because paraffin-embedded samples are widely available, rapid and reliable methods are needed for the isolation of nucleic acids, particularly RNA, from such samples."

Danenberg taught (paragraph [0014]) a method that "provides simple, efficient and reproducible methods for the isolation of RNA, DNA or proteins from tissue that has been embedded in paraffin."

Danenberg taught (paragraph [0022]): "Purified RNA can be used to determine the level of gene expression in a formalin-fixed paraffin-embedded tissue sample by reverse transcription, polymerase chain reaction (RT-PCR) amplification. Using appropriate PCR primers the expression level of any messenger RNA can be determined by the methods of the invention. The quantitative RT-PCR technique allows for the comparison of protein expression levels in paraffin-embedded (via immunohistochemistry) with gene expression levels (using RT-PCR) in the same sample."

Danenberg taught (paragraph [0034]): "Moreover, the technique can be applied to any of a wide range of tumor types and to an unlimited range of target genes. This has implications for the future preparation of individual tumor "gene expression profiles" whereby expression levels could be determined in individual patient samples for a range of genes that are known to influence clinical outcome and response to various chemotherapeutic agents. Automated real-time PCR from FFPE sample allows for the targeting of treatment to individual tumors."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to apply the method suggested by the combined teachings of Dai, Duvick, Clement, Lipson, Chang and Matsubara to samples of FFPE tissue using the RNA isolation method taught by Danenberg since, as Danenberg taught, these samples were widely available and allowed the comparison of protein expression levels with gene expression levels.

Response to Arguments

Applicant's arguments filed 05/26/2009 have been fully considered but they are not persuasive. Applicant argues (page 7, last paragraph):

In order for primers and probe that are specific for intron sequences to be useful in the methods of the present invention, the introns must meet two criteria a) the intron must be detectable and b) the intron must be correlated with prognosis or prediction as the case may be.

Dai taught the markers correlated with clinical outcome. Based on the disclosures of Duvick, Clement, Lipson, Chang and Matsubara, one of skill would have had a reasonable expectation that levels of intronic RNA for these genes would correlate with overall expression of the gene.

It is noted that:

Applicants do not agree that detecting intron sequences as provided in the disclosures provides a reasonable expectation of success in quantitatively detecting intron sequences as a measure of gene expression

On this point Applicant argues:

With regard to an intron being correlated with prognosis or prediction or being correlated with an exon which is correlated with prognosis or prediction, Duvick merely asserts (without presenting evidence) that in his experimental system, the spliced-out intron RNA would be *detected* at a level proportional to the transcription rate (emphasis added). In fact the spliced-out intron (as well as exons in the mRNA) would be *synthesized* at a level proportional to the transcription rate. To infer that the spliced-out intron RNA would be *detected* at a level proportional to the transcription rate, Duvick appears to assume that the degradation rate would be the same for the exon and for every spliced-out intron.

In fact, exons and introns are degraded independently.

This argument is not persuasive. Firstly, "transcription rate" can be considered a measure of gene expression, just as "steady state level of mRNA" or "level of protein" can be considered measures of gene expression (Dai paragraph [0127]: "The expression level may be determined by isolating and determining the level (i.e., amount) of nucleic acid transcribed from each marker gene."). These different measures of gene expression would not all produce the same "number", but each would be a reflection of "gene expression". Secondly, even if degradation of introns and degradation of mature mRNA do not proceed at the same rate, it would have been expected that each would have a characteristic half-life. Even if the half-life of introns (which half-life was "reasonable" according to Duvick) was shorter than the half-life of mRNA, Clement, Lipson, Chang and Matsubara were all clearly able to detect intronic RNA. That is,

even though the steady-state level of "intronic RNA" may have been expected to be lower than the steady-state level of mRNA for a particular gene, both "intronic RNA" and mRNA would have been expected to have steady-state levels dictated by the rates of synthesis and degradation. As such, each form would have been expected to correlate with the expression of the gene.

Applicant argues:

One of skill would not combine the references in the manner proposed by the Examiner to provide the claimed method because they would have no reasonable expectation that introns would be degraded at the same rate as exons and would therefore be useful for prognosis or prediction as the case may be.

As discussed above, introns and exons (mRNA) would not need to be degraded at the same rate for each to correlate with gene expression. mRNA and protein are certainly degraded at different rates, and yet each is used as a measure of gene expression (Dai paragraph [0130]). The point is that for a particular gene, the steady-state level of mRNA and the steady state level of a particular intron of the gene, though different, would each have been expected to correlate with the expression of the gene: the more highly expressed the gene, the more mRNA and the more intronic RNA from that gene would be present.

Applicant argues:

Furthermore, the method of Duvick is carried out in an experimental system, in which only the experimental variable, in this case the insertion site for the U-tag, is varied and in which other variables are controlled as closely as possible.

What the rejection relies on is not Duvick's artificial system, but rather his suggestion that introns are detected at a level proportional to the transcription rate of the genes they are in.

In conclusion, the examiner does not dispute that the steady-state level of intron-containing RNA (e.g. "free introns" resulting from splicing, or precursor RNA prior to splicing) would have been expected to be lower than the steady-state level of the exon-containing RNA (e.g. mature mRNA, or precursor RNA prior to splicing). It is also not disputed that different mechanisms are employed in the degradation of introns and mRNA. It is, however, the examiner's position that one of ordinary skill in the art would have expected, at the time the invention was made, that for any given intron sequence, a steady-state level would exist in the cell, and that this steady-state level would correlate with the expression of that particular gene, as suggested by Duvick. Therefore, because Duvick suggested that introns would be detected at a level proportional to the transcription rate, and because the other prior art cited in the rejection clearly showed that such intron sequences were detectable, it would have been obvious to target intron sequences for measuring gene expression in the method of Dai.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/
Examiner, Art Unit 1637

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637